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Immediate effects of cervical mobilisations on global perceived effect, movement associated pain and neck kinematics in patients with non-specific neck pain. A double blind placebo randomised controlled trial

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ABSTRACT

Background: Neck pain is prevalent, costly and disabling. Cervical mobilisations are frequently used to treat it but their effectiveness has been questioned by several systematic reviews. Evidence suggests that better outcomes are achieved with mobilisations when they are applied to specific patient subgroups. A criteria for patients suitable for neck mobilisations has been proposed, but the effectiveness on this patient subgroup has not been tested.

Objective: To assess the effectiveness of cervical mobilisations applied to a subgroup of patients with neck pain who fulfil specific criteria.

Design: Randomised controlled trial.

Method: 40 patients with neck pain attending a Physiotherapy clinic were recruited and randomised to a single session of either cervical mobilisations or motionless manual contact placebo. The immediate effects on global perceived effect, range of movement (ROM), movement velocity and movement associated pain were assessed.

Results: mobilisation participants reported significantly better global perceived effect ($p<0.001$) and improvements in movement associated pain ($p=0.041$). Mobilisations produced a significant increase in ROM in side flexion ($p=0.006$) and rotation ($p=0.044$) when compared with placebo, but only in patients with pre-intervention ROM restriction. 29-47% of all movement associated pains were resolved following mobilisations and 11-27% following placebo. Patients in both groups showed a significant ($p<0.05$) increase in movement velocity, but only in those who had a velocity restriction pre-intervention.

Conclusions: Cervical mobilisations are effective in improving movement-associated pain, increasing ROM and velocity, and patient perceived improvement when applied to patients with neck pain that fulfil a criteria. Their use should be advocated.

Keywords: cervical, mobilisations, placebo, neck pain.

1. INTRODUCTION

Neck pain has a high prevalence¹ and has been ranked the 4th greatest contributor to global disability². Cervical mobilisations - low velocity passive oscillatory movements³, are frequently used to treat neck pain^{4,5}, but their effectiveness has been questioned by recent systematic reviews⁶⁻⁸. The heterogeneity of participants in randomised controlled trials (RCT) has been suggested as an explanation for the lack of positive findings as an effect in a subgroup of patients may be diluted by the absence of an effect in others^{9,10}. Evidence suggests that treatment outcomes with cervical mobilisations are improved when their application is based on patient subclassification¹¹⁻¹³. Hence, the identification of characteristics marking those most suited for cervical mobilisations has been recommended^{14,15}. Clinical criteria defining patients appropriate for mobilisations have been proposed¹⁶, but their validity have yet to be tested.

Clinical trials in manual therapy have been criticised for making an inadequate use of sham interventions and underestimating the placebo effect¹⁷⁻¹⁹. The placebo effect is low when participants are aware that placebo is one of the treatment arms²⁰ and greater with instructions that enhance their expectations²¹ and they believe they have received an effective treatment^{22,23}. It has been recommended that the context, patient expectations and the interaction between provider and participant be considered when conducting trials of manual therapy¹⁸.

The primary aim of this study was to assess the short term effectiveness of cervical mobilisations applied to a specific subgroup of patients with neck pain. Secondary aims were to assess if further patient or clinical characteristics may be associated with the effectiveness of mobilisations, and to assess the magnitude of the placebo effect as a possible mechanism of action of cervical mobilisations.

2. METHODOLOGY

Following ethical approval (M10_2016_095), a double-blind RCT was conducted (ClinicalTrials.gov record number: X). Data collection took place at a Physiotherapy clinic between September 2016 and August 2017.

2.1. Participants

Forty participants (20 in each group) were required to detect a difference in clinical outcome with a power of 80% and α 0.05 if patients in the mobilisation group were three times more likely to be classified as responders than those in the placebo group. Patients with pain between the superior nuchal line and first thoracic spinous process of any duration and attending a physiotherapy clinic were invited to participate. They were included if they experienced symptoms where mobilisations were indicated according to predefined criteria¹⁶ (Table 1). Exclusion criteria were a whiplash injury, had or were awaiting neck surgery, or had been diagnosed with an inflammatory disease or spinal condition (Figure 1).

In order to prevent patient expectation affecting outcome^{22,23}, patients were not informed of the existence of a placebo but were advised that the effectiveness of two treatments was being assessed.

2.2. Procedure

Following informed consent, patients' age, gender, duration of symptoms (classified as chronic if duration was >12 weeks, otherwise as acute/subacute^{5,24}), height, weight and handedness were recorded, and they completed the Neck Disability Index (NDI) questionnaire²⁵. The NDI is the most commonly used, reliable and validated self-report instrument to evaluate neck disability²⁶; it consists of 10 questions, total scores ranging 0-100, higher scores representing greater disability²⁷. In addition, patients were asked to draw their painful area on a body chart and to rate the maximum and average pain intensity in the last 24 hours using an 11 point numeric pain rating scale²⁸ with 0 representing "no pain" and 10 representing "worst pain imaginable".

Immediately before and after the intervention, 3D neck movement was measured during three repetitions each of neck flexion, extension, left and right rotation, and left and right side flexion (Figure 2), performed at self-selected speeds. Patients were advised to move their neck as far as they were able. If pain occurred they were instructed to raise their left thumb and lower it when pain subsided.

After intervention, patients were asked to rate their global perceived effect to the intervention using the Global Rating of Change Scale (GROC)²⁹. GROC is a 15-point scale ranging from -7 (a very great deal worse), through 0 (no change), to +7 (a great deal better)³⁰. It is widely used to evaluate change in neck pain³⁰⁻³³ because of its validity and clinical relevance, and correlation with self-rated importance of change and patient satisfaction measures³⁴, and has been recommended to be used as a core outcome measure by the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials³⁵.

2.3. Neck Kinematics

A 6 camera Vicon motion capture system (Vicon Systems Ltd., Oxford, UK) was used to measure neck 3D kinematics. Reflective 14 mm markers were attached using double-sided tape to the bridge of nose, chin midpoint, right and left tragus, xiphoid process, suprasternal notch, external occipital protuberance, spinous processes of the first and eighth thoracic vertebrae, and the left thumb. Head and thorax coordinate systems were defined according to Koerhuis, et al.³⁶ and Guo, et al.³⁷. Raw data was filtered with a 4th order low-pass filter with a cutoff frequency of 6 Hz³⁸. This method has shown high reliability for the measurement of neck 3D movement and associated pain.³⁹.

2.4. Interventions

Patients were randomly allocated to either cervical mobilisations or placebo using concealed randomisation⁴⁰. After assessment for suitability and all baseline data had been recorded, the treating physiotherapist opened an opaque sealed envelope that specified the group allocation. Participants were blind to their group allocation. A separate investigator took all measurements and was unaware of the patient's treatment allocation until all data analysis was complete.

In the mobilisation group, the physiotherapist performed grade II-III segmental postero-anterior and/or antero-posterior mobilisations following the movement plane of the cervical zygapophyseal joints (downslope or upslope)^{16,41} with the patient in supine. Mobilisation level was selected according to clinical reasoning and targeted at segments that reproduced the symptoms and/or were identified as hypomobile during examination. For the placebo group, the same hand position as for the mobilisations was utilised but without performing the accessory glide. In order to limit the effect of therapist and patient interaction on treatment outcome^{42,43}, patients in both groups were asked about discomfort and symptom reproduction during the interventions. The intervention lasted 10 minutes in both groups. The same physiotherapist with 13 years clinical experience and postgraduate training in neuromusculoskeletal physiotherapy performed both interventions.

2.5. Data analysis

The effectiveness was evaluated using GROC, presence of pain during neck movements, ROM and neck movement velocity.

Difference in the categorical distribution of GROC was tested with the Mann Whitney test. Patients were also classified into responders or non-responders using GROC. They were classified as responders if they reported to be at least "somewhat better" after the intervention⁴⁴; all other patients were classified as non-responders. The effectiveness of interventions (placebo vs mobilisations) on global perceived effect (responders vs non-responders) was assessed using a binary logistic regression. The model was adjusted for the effect of confounding variables⁴⁵, which had been identified as having an univariate relationship with global perceived effect using t tests for continuous variables and chi-square tests for categorical variables⁴⁶; confounding variables were retained in the model if they caused $\geq 10\%$ change in the regression β ⁴⁷. In order to identify which pre-intervention patient characteristics were predictive of intervention effectiveness (global perceived effect), baseline variables (age, average pain intensity, maximum pain intensity, body mass index, duration of symptoms and number of painful movements) were dichotomised and the odd ratios estimated through logistic regression. For the dichotomisation of maximum and average pain intensity the mean of the sample (7 and 5 respectively) were taken as cut-off points to divide patients into either having high or low pain intensity. Due to lack of statistical power, the interaction between NDI and intervention could not be assessed with logistic regression, and therefore an independent samples t test was used to test for differences in NDI between responders and non-responders in each group.

The effect on ROM was assessed using two-way ANCOVAs, with change (post-intervention minus pre-intervention) as the dependent variable, intervention and presence of ROM restriction as independent factors, and pre-intervention ROM as covariate. Restriction in side flexion and rotation was defined as an asymmetry of at least 10% with the contralateral movement. For flexion and extension, restriction was defined as a 10% reduction in ROM with respect to normative data collected in a previous study⁴⁸, where participants demonstrated an average flexion and extension movement of 47° and 51° respectively. Post hoc analysis of within-group changes were performed using Paired t tests.

The effect on movement velocity was tested using two-way ANCOVAs, with velocity change (post-intervention minus pre-intervention) as the dependent variable, intervention and presence of velocity restriction as independent factors, and pre-intervention velocity as covariate. Velocity restriction in side flexion and rotation was defined as an asymmetry of $\geq 10\%$ with the contralateral movement; for flexion and extension, as an asymmetry of at least 10% with regards to extension and flexion movements respectively. Post hoc analysis of within-group changes in velocity were performed using Paired t tests.

The effect on movement associated pain was assessed using one-way ANCOVA, with change in number of painful movements (post-intervention minus pre-intervention) as the dependent variable, intervention as the independent factor and pre-intervention number of painful movements as covariate.

3. RESULTS

Patient characteristics are shown in Table 2.

Global rating of change scale

Following the intervention, 80% of patients in the mobilisation group and 45% of patients in the placebo group reported improvement (“a tiny bit better” or greater) (Figure 3). The magnitude of improvement was greater in the mobilisation group ($p < 0.001$); medians in the GROG scale following mobilisation and placebo were 11.5 and 8 respectively, equivalent to feeling “somewhat-moderately” better and “about the same”. Patients in the mobilisation group were more likely to be classified as responders (adjusted odds ratio: 11.7; 95% IC: 2.29-59.86; $p = 0.003$). Having maximum pain $\geq 7/10$, average pain $\geq 5/10$, a normal BMI and > 4 painful movements increased the odds of successful outcome following mobilisation (Figure 4). Patients who responded to mobilisations had a higher NDI than non-responders (mean difference: 14.54; 95% CI: 3.26-25.83; $p = 0.014$). There were no differences in NDI between responders and non-responders in the placebo group.

Pain during movement

Following intervention, pain during side flexion in the mobilisation and placebo groups was resolved in 29% and 16% of patients who experienced pain pre-intervention, pain during rotation in 36% and 11%, pain during flexion in 36% and 27% and pain during extension in 47% and 23% respectively. The number of painful movements resolved in each patient was greater following mobilisations (placebo: 0.6, 95% CI: 0.1-1.2; mobilisations: 1.5, 95% CI: 0.9-2; $p=0.041$).

Range of movement

Side flexion

Twenty-three patients were classified as having a side flexion restriction of $25.2 \pm 12.32\%$ (mean \pm SD) with respect to the contralateral side. There was a main effect of intervention ($p=0.006$) and a significant interaction for intervention \times presence of ROM restriction ($p=0.015$). Baseline ROM showed a significant contribution to the model ($p=0.003$). Post-hoc analysis revealed a significant difference in Δ ROM between intervention and placebo only in patients with a pre-intervention restriction (mean difference: 5.2° ; 95% CI: 1.84-8.56; $p=0.002$) (Figure 5A).

Rotation

Twenty patients were classified as having a rotation restriction of $21.37 \pm 11.17\%$ with respect to the contralateral side. There was a main effect of intervention ($p=0.044$) but the interaction intervention \times presence of ROM restriction was not significant ($p=0.089$). Baseline ROM contributed significantly to the model ($p<0.001$). Post-hoc analysis revealed a significant difference in Δ ROM between groups only in those with a pre-intervention restriction (mean difference: 4.8° ; 95% CI: 0.32-9.28; $p=0.035$) (Figure 5B).

Flexion and Extension

Twenty patients were classified as having an extension restriction of $33.51 \pm 13.78\%$ compared to normative values. Eight were classified as having a flexion restriction of $23.15 \pm 15.05\%$. There were no differences in Δ ROM post-intervention between groups. No other effects or interactions were noted.

Velocity

There were no differences in velocity change between groups. There was a significant association between pre-intervention and post-intervention velocity for all movements ($p<0.004$). Post-hoc analysis revealed that velocity improved post-intervention in both groups for side flexion, rotation and flexion, and only in the mobilisation group for extension; however such improvement was only observed in patients that demonstrated a velocity restriction at baseline (Table 3).

4. DISCUSSION

The context of the treatment including patient expectations, therapist's behaviour, environment, and therapist-patient interaction have been found to contribute to treatment outcomes^{17,20,21,49,50}. Where possible, this study attempted to control for these factors so that differences in outcome could be attributed to the intervention. We found mobilisations to have greater immediate benefit than placebo in global perceived effect, movement associated pain and ROM.

Patients in the mobilisation group were 12 times more likely to be classified as responders than those receiving placebo, suggesting a large effect⁵¹. Our findings regarding GROC are in agreement with Izquierdo Perez, et al.³² who also reported participants feeling "somewhat" or "moderately" better following cervical mobilisations. Although reduction in pain intensity has been previously reported⁵²⁻⁵⁶, to our knowledge this is the first study to assess immediate resolution of movement associated pain following mobilisations. Resolution of pain is most likely due to the activation of pathways associated with mechanical hypoalgesia at the central nervous system¹⁹ although changes in neck muscle activity (which may normalise neck loading and/or abolish myogenic pain) have also been reported following cervical mobilisations^{56,57}.

The increase in ROM in patients with movement restriction is in agreement with Izquierdo Perez, et al.³² and Kanlayanaphotporn, et al.⁵³ who found improvements in ROM of a similar magnitude, but contrasts with the findings of other studies that reported no short term improvement in ROM following cervical mobilisations^{52,58}. Unlike these studies, patients in our study were classified as having a movement restriction in side flexion and rotation if they presented with $\geq 10\%$ asymmetry, and it is in this subgroup where the greatest improvements in ROM were observed. Although a 10% asymmetry may be considered minor, these findings suggest that the effectiveness of mobilisations in Δ ROM is dependent upon the presence of a restriction pre-treatment, and no change is likely with no initial restriction. It is not known if participants in the study by Izquierdo Perez, et al.³² and Kanlayanaphotporn, et al.⁵³ also showed a pre-treatment restriction that may have favoured a treatment effect. Nevertheless, the magnitude of ROM improvements observed was of limited clinical importance, just below (rotation) and above (side flexion) the minimum detectable change^{39,59}. Patients presented with an average restriction of 25% and 21% of ROM in side flexion and rotation respectively, greater improvements may have been seen if they had shown greater restriction. There were no improvements in ROM in flexion or extension. The mobilisation techniques used in this study may preferentially produce a movement increase in the transverse and frontal planes, rather than sagittal plane. Evidence suggests that the cervical spine is more sensitive to the type of technique used than the lumbar spine⁶⁰. Alternatively, the criteria used to classify patients as having a movement restriction in flexion and extension (calculated as ratio of asymptomatic subjects' data collected previously) may not be appropriate and a within-subject restriction classification similar to that used in side flexion and rotation may be required.

We used a longer treatment duration than previous studies^{32,52,53,58}, which have ranged between 3 and 8 minutes. Some of the differences between our findings and previous studies may be attributed this as there is evidence that greater effects may be expected from higher dosages⁶¹⁻⁶³. Although Izquierdo Perez, et al.³² obtained similar results to ours using a lower

dosage (6 minutes), our subjects had greater disability and pain intensity, which may have required a higher dosage of mobilisations.

Movement velocity increased in both groups and all movements (except extension in placebo), but only in those patients where an asymmetry in movement velocity pre-intervention was noted. Decreased movement velocity in neck pain has been correlated with kinesiophobia^{64,65} and fear of pain⁶⁶. The observed increase in velocity in both groups may be secondary to a decrease in these following intervention. Since no differences between groups were observed, changes in movement velocity may be attributed to a placebo effect. It is of note that the placebo intervention also produced a considerable improvement in symptoms. The effects of mobilisations may partly be mediated by a placebo effect through context-induced positive expectation and conditioning, which have been found to activate a descending pain modulating network in the central nervous system (known to modulate the ascending nociceptive inputs) through the activation of the endogenous opioid and endocannabinoid systems⁶⁷⁻⁶⁹.

We found further clinical features associated with the effectiveness of mobilisations in GROC. Patients who had a higher NDI, average and maximum pain, and a greater number of painful movements were more likely to benefit from mobilisations, whereas patients who presented with a lower severity condition (lower NDI, average and maximum pain, and <4 painful movements) were equally likely to benefit from mobilisations and placebo. This is in agreement with a previous study that found higher neck pain intensity to be predictive of better outcome following cervical manipulation⁷⁰, but in contrast with another where a higher NDI was associated with a poorer outcome³⁰. Notably, the former had an inclusion criteria similar to ours (primary complaint of mechanical neck pain; radiculopathy excluded) whereas the latter also included patients with cervical radiculopathy, myofascial pain and cervicogenic headache.

Our findings support the use of mobilisations in patients with mechanical neck pain who fulfil the criteria outlined in this study. Although criteria for cervical mobilisations published earlier¹⁶ suggest that these may be better suited to treat patients with a limited symptom duration, in our patients symptom duration (either acute/subacute or chronic) made no difference to treatment effectiveness. Symptom duration appears to influence the effectiveness of cervical²² and thoracic⁴⁶ manipulations in neck pain but we found no evidence of such effect with mobilisations, although differences in the definition of symptom duration may partly account for this. Having a normal BMI (as opposed to being overweight or obese) also increased the odds of successful outcome following mobilisations. Although BMI has been found not to affect the spontaneous recovery from neck pain⁷¹ or long term treatment outcomes following a multimodal physiotherapy intervention for neck pain⁷², our findings suggest that it has a moderating role on the short term effectiveness of mobilisations.

The criteria for mobilisations published earlier¹⁶ limited the application of mobilisations to patients with spinal movement patterns suggestive (through active and passive examination) of a movement restriction local to one or two functional spinal units. Due to the questioned reliability of the examination techniques currently used to localize intervertebral hypomobility^{73,74} and the lack of any substantial evidence that cervical monosegmental

conditions may be better suited for mobilisations, we did not include such clinical feature in our inclusion/exclusion criteria.

5. STUDY LIMITATIONS

This study assessed the short-term effects and immediate changes in pain, ROM and global perceived effect have been found to predict improvements in the longer term^{44,75-77}. However further research in the long term effects in this specific subgroup is warranted. Although mobilisations were found effective in patients who fulfilled the criteria, it is not known if they may be useful to differentiate between those patients who do or do not benefit from mobilisations. Further research is required to validate the criteria. This study was not powered to perform a secondary analysis of outcome predictor variables and therefore conclusions regarding predictors must be considered with caution. Therapist's treatment preferences have been found to affect treatment outcome⁷⁸ and we were unable to control for this, which may have favoured a better outcome in the mobilisations group. We used manual contact to assess the placebo effect, however touch has been found to have an analgesic effect by a gating of the ascending nociceptive afferent input at subcortical level, especially if the area of stimulation is close to the source of pain⁷⁹. Therefore, it is likely that, to some extent, the improvements in symptoms reported by patients in the placebo group may have been caused by the analgesic effect of touch.

5. CONCLUSION

Cervical mobilisations are more immediately effective than placebo in global perceived effect, movement associated pain and ROM when these are applied to a subgroup of patients with neck pain who fulfil these specific criteria, and therefore their use in treatment is advocated. ROM and velocity gains should only be expected in patients who show a pre-treatment restriction. Patients with a more severe neck condition and a lower BMI may be more suited for mobilisations. Our findings do not support the preferential use of mobilisations in acute conditions. Improvements observed in the placebo group suggest that the effectiveness of mobilisations may, in part, be associated with a placebo effect.

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Table 1: Inclusion criteria

Primary complaint of neck pain
Non-traumatic history of onset
Mechanical in nature
Pain has a clear mechanical aggravating and easing positions or movements (e.g. neck rotation and extension)
Limited range of motion ($\geq 10\%$ compared to contralateral rotation/side flexion, or normative data in flexion/extension)
Local provocation tests produce recognisable symptoms
No neurological deficit
No signs of central hyperexcitability
Referral to other health professional to exclude red flags not required
A positive expectation that mobilisations will help

Table 2: Participant characteristics at baseline. Values are mean \pm SD or number of cases (/)

	Mobilisation	Placebo
Age (years)	43.9 \pm 16	45.5 \pm 14
BMI	24.5 \pm 4.1	26 \pm 4.3
Gender (F/M)	14/6	10/10
Handedness (R/L)	17/3	19/1
Duration of neck pain (years)	7.6 \pm 10.6	5.4 \pm 6.5
Acute/Chronic	6/14	6/14
NDI score	26.3 \pm 12.7	22.8 \pm 14.4
Are of pain (Bilateral/Right/Left)	12/7/1	8/6/6
Maximum pain	7.2 \pm 1.3	6 \pm 1.9
Average pain	5.1 \pm 1.2	4.3 \pm 1.8
Side flexion ROM (degrees)	26.9 \pm 8.6	33.7 \pm 10.5
Rotation ROM (degrees)	48.8 \pm 14	55 \pm 7.4
Flexion ROM (degrees)	46 \pm 10.03	51.2 \pm 7
Extension ROM (degrees)	40 \pm 11.5	46.2 \pm 11.2
Pain during side flexion (Y/N)	18/2	18/2
Pain during rotation (Y/N)	18/2	15/5
Pain during flexion (Y/N)	14/6	11/9
Pain during extension (Y/N)	15/5	13/7
Side flexion velocity (degrees/second)	14.2 \pm 7.4	19.2 \pm 6.8
Rotation velocity (degrees/second)	29.7 \pm 16.5	35.1 \pm 14.7
Flexion velocity (degrees/second)	17.2 \pm 8.7	22.1 \pm 6.2
Extension velocity (degrees/second)	16.8 \pm 7.7	22.4 \pm 8.2

Table 3: Change in movement velocity post intervention (degrees/second)

	Group	Baseline restriction	Mean difference \pm SD	95% CI
Side flexion	Mobilisation	Restriction	3.4 \pm 3.6	1.6-5.3 **
		No restriction	1 \pm 5.2	-1.3-3.3
	Placebo	Restriction	2.8 \pm 4.4	0.3-5.4 *
		No restriction	0.8 \pm 4.5	-1.1-2.7
Rotation	Mobilisation	Restriction	4.9 \pm 8.4	0.1-10 *
		No restriction	-2.2 \pm 11.5	-2.4-6.7
	Placebo	Restriction	5.27 \pm 7.99	0.45-10.10 *
		No restriction	1.3 \pm 9.5	-2.5-5
Flexion	Mobilisation	Restriction	6.7 \pm 4.7	2.8-10.6 **
		No restriction	1.4 \pm 5.5	-2.1-4.9
	Placebo	Restriction	7.1 \pm 5.6	3.1-11.1 **
		No restriction	0.1 \pm 3.5	-2.6-2.4
Extension	Mobilisation	Restriction	2.6 \pm 3.3	0.1-5.1 *
		No restriction	1.3 \pm 4.5	-1.7-4.3
	Placebo	Restriction	2.2 \pm 4.1	-1.6-6
		No restriction	0.5 \pm 4.5	-2.2-3.3

*p < 0.05; **p < 0.01

Figure 1: CONSORT flow diagram

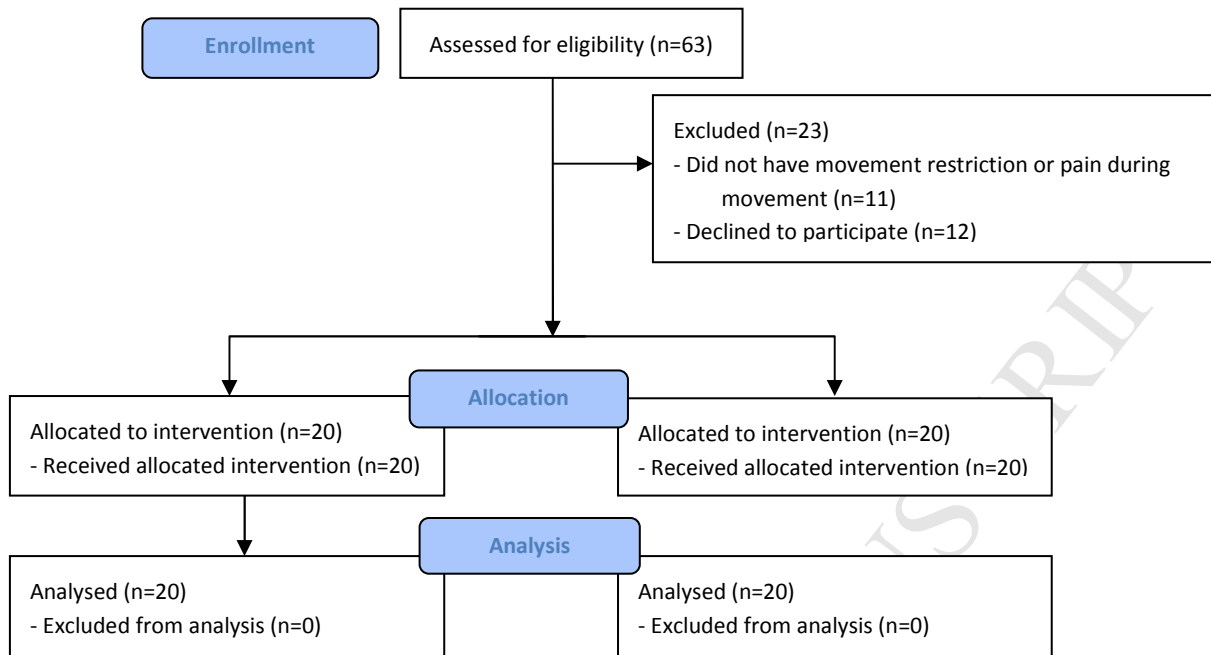


Figure 2: Neck movements tested

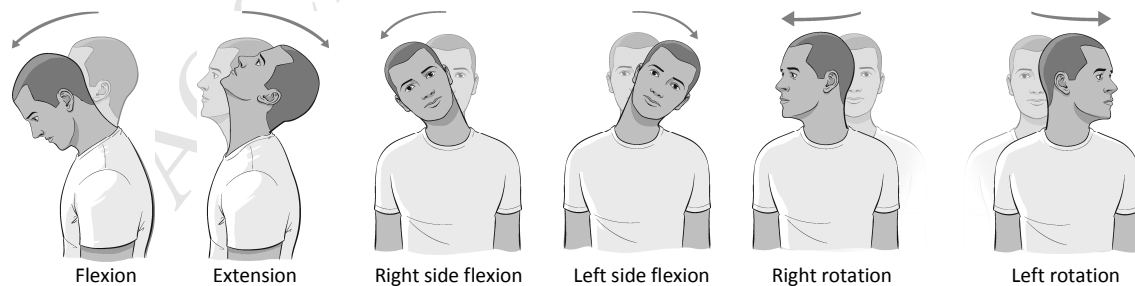


Figure 3: Patient perceived improvement (GROC scale) following intervention

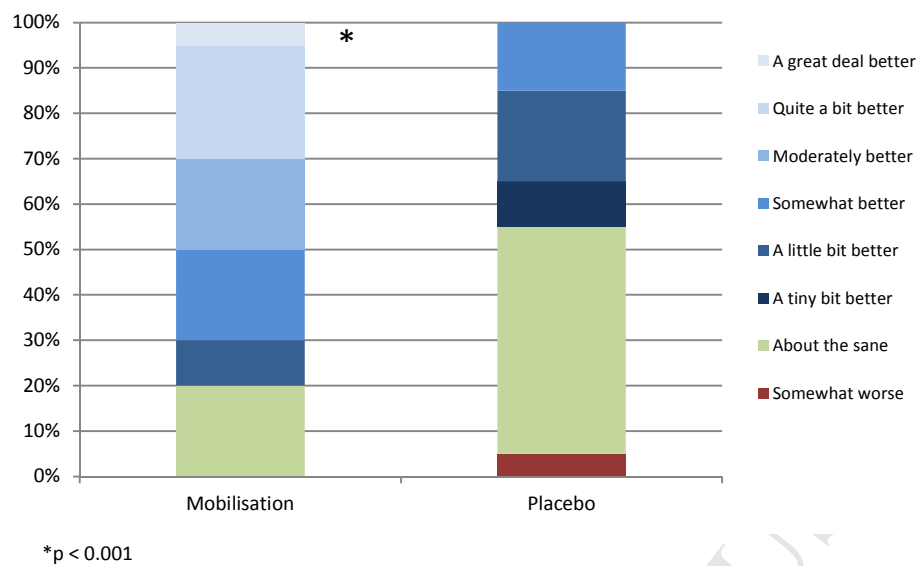


Figure 4: logistic regression; effect of baseline variables on treatment outcome (responder or not responder)

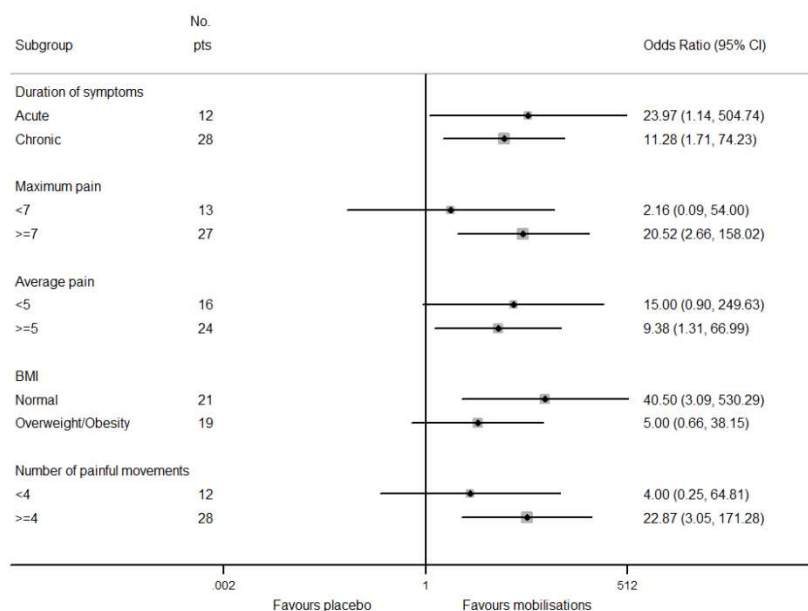
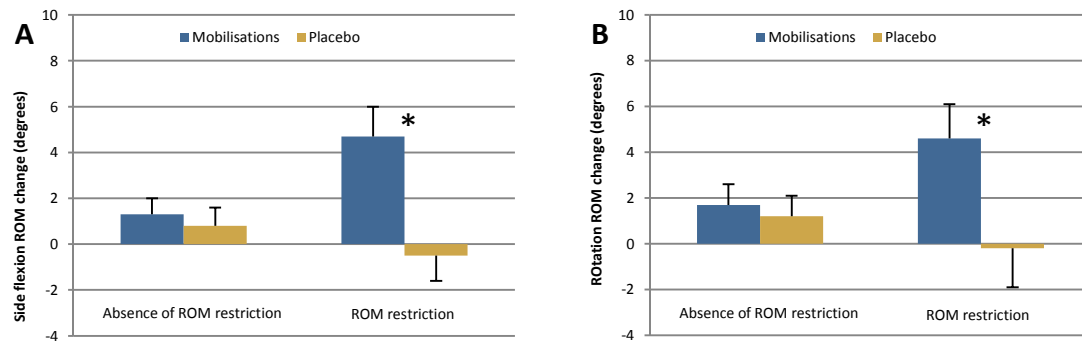


Figure 5: ROM change from pre to post intervention (estimated marginal mean and standard error) for side flexion (A) and rotation (B).



HIGHLIGHTS

- Cervical mobilisations are effective in reducing symptoms in patients with neck pain
- Improved range of movement should only be expected in patients with restricted movement
- The effects of mobilisations are, to some extent, mediated by a placebo effect